

**Award Number:** W81XWH-07-1-0283

**TITLE:** PR064845: Predictors of Treatment Response to Fluoxetine in PTSD Following a Recent History of War Zone Stress Exposure

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Temple, TX 76504

**REPORT DATE:** July 2011

**TYPE OF REPORT:** Annual

**PREPARED FOR:** U.S. Army Medical Research and Materiel Command  
Fort Detrick, Maryland 21702-5012

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14. ABSTRACT: Although selective serotonin reuptake inhibitors (SSRIs) are routinely prescribed for acute stress disorder and early PTSD and recommended in the VA-DoD best practice guidelines, the efficacy of SSRIs as an early intervention for PTSD in service members returning from war-zone duty has still not been determined. Consequently, this study was designed to conduct a controlled trial of fluoxetine as an early intervention for recently redeployed soldiers, as well as to develop methodologies for understanding the multiple factors that may predict outcome. The Brooke Army Medical Center IRB, the regional IRB for the Carl R. Darnall Army Medical Center, has given full approval. A CRADA between TEMPVA Research Group, Inc and the Carl R. Darnall Army Medical Center has been executed. Human Research Protection Office (HRPO) Office of Research Protections (ORP) U.S. Army Medical Research and Materiel Command (USAMRMC) Fort Detrick has been completed and full approval has been given for enrollment. Continuing review was approved in April 2011. 35 participants have been enrolled and recruitment continues. A second performance site, the Central Texas Veterans Health Care System, is being added to aid recruitment. A no-cost extension continues until June 30, 2012.					
15. SUBJECT TERMS Fluoxetine, Posttraumatic Stress Disorder, Antidepressants					
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**INTRODUCTION:**

Although selective serotonin reuptake inhibitors (SSRIs) are routinely prescribed for acute stress disorder and early PTSD and recommended in the VA-DoD best practice guidelines, the efficacy of SSRIs as an early intervention for PTSD in service members returning from war-zone duty has still not been determined. Consequently, this study was designed to conduct a controlled trial of fluoxetine as an early intervention for recently redeployed soldiers, as well as to develop methodologies for understanding the multiple risk factors that may predict outcome. Fluoxetine was selected as the psychopharmacologic agent for this study because it is well tolerated, it has a very favorable cost-benefit advantage as a generic drug, and the fact that it is the only SSRI with at least preliminary studies demonstrating its efficacy in recent-onset, war-related PTSD. Studies focusing on targeting chronic combat-related PTSD with SSRIs have shown mixed results with some small open-label studies suggesting efficacy, while two controlled trials with Vietnam veterans were negative. In a recent study of survivors of war violence in Europe, Israel, and South Africa, fluoxetine was shown to significantly reduce PTSD symptoms. Because in all prior trials there is considerable variability of response to fluoxetine, we plan to examine several predictors of efficacy. We argue that the efficacy of SSRIs for recently redeployed soldiers at risk for chronic PTSD is moderated by multiple personal, deployment, and environmental factors. It is expected that not all subjects will respond to fluoxetine. For those that do not respond to fluoxetine alone, augmentation with either buspirone or bupropion will be offered based on their reasonable tolerability, low cost and the recent findings documenting their utility as adjunctive treatments for depression.

**BODY:**

The approval letter has been received from the Brooke Army Medical Center IRB, the regional IRB for the Carl R. Darnall Army Medical Center. The CRADA between TEMPVA Research Group, Inc. and CRDAMC has been executed. The protocol has been approved by the Central Texas Veterans Health Care System IRB and the Research and Development Committee. The Human Research Protection Office (HRPO) of the Office of Research Protections (ORP) U.S. Army Medical Research and Materiel Command (USAMRMC) Fort Detrick has given full approval for initiation of the study. We continue to use the VA-donated administrative trailer (12'X52') to provide sufficient office space to perform the study. Ninety potential participants have been presented with information regarding the study. Of those, 35 signed a consent form. Of the 35 that signed a consent form, 15 met exclusion criteria, 4 did not complete inclusion/exclusion assessments and therefore did not qualify, and 16 have been randomized. Of the 16 randomized, 7 have been lost to follow-up and 4 withdrew for personal reasons after completing part of the trial, 3 have completed all 32 weeks of the trial (Phase I and Phase II), and 2 are in active treatment (1 has completed week 16 assessments and 1 is in the first month of treatment). Clearly, we are experiencing much more difficulty recruiting than anticipated. We have addressed this by individual meetings with key administrators of clinical programs, grand rounds presentations to Ft. Hood mental health clinicians, and using flyers and pamphlets, approved by the BAMC IRB, which have been placed in strategic places on the Ft. Hood campus. A public service announcement on the Ft. Hood public television network has been prepared and distributed. The most successful strategy for recruitment has been use of the flyers. We continue to investigate ways to make sure that the basic information regarding the project is available to

individuals that may be appropriate for participation. Because of these difficulties we have requested and received IRB approval from both the BAMC and VA IRBs to add the Central Texas Veterans Health Care System (CTVHCS) as a second site. CTVHCS offers advantages to us because one of the psychiatrists working on this project, Dr. Pazzaglia, is a primary provider in the CTVHCS PTSD Clinical Team in Temple. She can assist in recruiting participants from her clinics and has a very good working relationship with other providers in that clinic.

Two research assistants continue to work on this project. One has a master's degree in counseling psychology and the other has a Ph.D. in counseling education. Both have considerable clinical experience, as well as some research experience. They have been trained on the administration of the psychological tests associated with this project and have developed the casebooks used in data collection, as well as been trained on the use of the CRDAMC electronic medical record system. Credentialing and privileging of Drs. Peggy Pazzaglia and Paul Hicks at the Carl R. Darnall Army Medical Center has been completed and renewed. The Boston VA team under the leadership of Dr. Brett Litz has been assisting in the preparation of the database for recording of the participant data.

The continuing review from the BAMC and VA IRBs has been approved (see Appendix). PR064845 is registered in ClinicalTrials.gov, No. NCT00633685.

#### Project Tasks:

##### Task 1: Submission of the Proposal to the IRBs

- The proposal must be approved by both the Brooke Army Medical Center IRB and the Central Texas Veterans Health Care System Human Subjects Subcommittee.
- **Completed**

##### Task 2: Recruitment and Training of Study Personnel

- Hire two master's prepared research assistants
- Training on recruitment procedures and research assessments (SCID, CAPS, etc.)
- **Completed**

##### Task 3: Preparation of Over-Encapsulated Blinded Medications for the First Phase of the Clinical Trial

- Purchase of the fluoxetine and gelatin capsules from VA pharmacy suppliers (purchased each 3 months throughout the first 15 months of the study)
- Over-encapsulation of fluoxetine and empty gelatin capsules by CTVHCS Pharmacy staff
- Transfer of medications prepared by the CTVHCS Pharmacy directly to the Carl R. Darnall Medical Center Pharmacy
- The Fluoxetine and placebo capsules have been prepared and transferred to the CRDAMC Pharmacy.
- **Completed**

##### Task 4: Recruitment/Clinical Trial

- Enrollment of a minimum 20 subjects per month for 15 months
- Double-blind, placebo-controlled trial of fluoxetine + usual psychological care for 12 weeks
- Open-label extension of the fluoxetine trial for 20 weeks
- **In progress**

Task 4: Data Collection and Transfer to the Boston VA National PTSD Research Center

- Data will be stored on compact discs for storage
- Compact discs will be sent on a monthly basis to the National PTSD Research Center for database development
- The post-doctoral fellow working with Dr. Brett Litz will maintain the database under the oversight of Dr. Litz

Task 5: Data Analysis at the Boston VA National PTSD Research Center

**KEY RESEARCH ACCOMPLISHMENTS:** Recruitment continues.

**REPORTABLE OUTCOMES:** Not applicable.

**CONCLUSIONS:** Not applicable.

**REFERENCES:** Not applicable.

**APPENDICES:**

Appendix A: BAMC IRB Continuing Review Approval letter, Approved Informed Consent Document, and HIPAA Consent Form

Appendix B: CTVHCS IRB Continuing Review Approval letter

Appendix C: No-Cost Extension of Award Contract

Appendix D: Recruitment Flyer

Appendix E: Recruitment Pamphlet

**SUPPORTING DATA:** Not applicable





**DEPARTMENT OF THE ARMY  
BROOKE ARMY MEDICAL CENTER  
3851 ROGER BROOKE DR.  
FORT SAM HOUSTON, TX 78234**

REPLY TO  
ATTENTION OF:

MCHE-CI

May 9, 2011

MEMORANDUM FOR: Michael Adams, PhD  
FROM: Brooke Army Medical Center (BAMC) Institutional Review Board  
  
PROJECT TITLE: [363502-7] "Predictors of Treatment Response to Fluoxetine in PTSD following a recent history of war zone stress exposure {CDMRP}," C.2007.145  
REFERENCE #: C.2007.145  
SUBMISSION TYPE: Response/Follow-Up  
  
ACTION: APPROVED  
EFFECTIVE DATE: May 9, 2011

1. Thank you for submitting the Response/Follow-Up to the IRB stipulations from the Continuing Review of 1 Dec 2010 for the above research study. The Brooke Army Medical Center (BAMC) Institutional Review Board has APPROVED your submission on 9 May 2011 under the expedited pathway, in accordance with 21 CFR 219.110. This protocol will expire 30 Nov 2011 and the next continuing review will be due in 11 months. No further action on submission 363502-7 is required at this time.

2. The following item was acknowledged in this submission:

- Continuing Review/Progress Report - IRB requested changes (UPDATED: 04/15/2011)

3. If you have any questions, the POC is Brenda C. Torres at (210) 916-2598 or [brenda.torres2@us.army.mil](mailto:brenda.torres2@us.army.mil). Please include your project title and reference number in all correspondence with this committee.

This document has been electronically signed in accordance with all applicable regulations, and a copy is retained within our records.

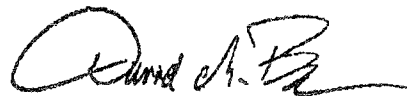


APR 08 2011

MEMORANDUM FOR Michael Adams, PhD, C. R. Darnall Army Medical Center

SUBJECT: Continuing Review of the protocol entitled “**Predictors of Treatment Response to Fluoxetine in PTSD Following A Recent History of War Zone Stress Exposure.**”  
**C.2007.145**

1. The Brooke Army Medical Center (BAMC) Institutional Review Board (IRB) met on 01 Dec 2010 **conditionally approved** the continuation of the protocol.
2. The IRB requests the following:
  - a. **In the Progress Report:**
    - In the deviation section of the progress report, add an additional deviation to reflect the current submissions on record.
3. The items requested above are due in the DCI Protocol Office by **COB, 8 May 2011** or your protocol will be terminated and notice sent to the Deputy Commander.
4. POC is the Protocol office at (210) 916-7394/4039.



DAVID BUSH  
Lt Col, USAF, MC  
HPA, BAMC IRB

Adams  
C. 2007.115

MCHE-CI

MEMORANDUM FOR Principal Investigator

SUBJECT: Latest Approved Informed Consent Form

1. Attached please find the reviewed Consent Form with approval stamp date. You must begin using a copy of this Consent Form with the approved stamp to document informed consent of all subjects.
2. Any future changes to Consent Form must be submitted and approved by the Institutional Review Board (IRB) before use.

Brooke Army Medical Center  
Protocol Office

**BROOKE ARMY MEDICAL CENTER/CARL R. DARNALL ARMY MEDICAL CENTER  
INFORMED CONSENT DOCUMENT  
Predictors of Treatment Response to Fluoxetine in PTSD Following a Recent History of War  
Zone Stress Exposure**

**Site Principal Investigator:** Michael L. Adams, Ph.D., LTC (Ret.)

**Principal Investigator:** Paul B. Hicks, M.D., Ph.D. (Central Texas Veterans Health Care System;  
Temple, Texas)

**Research Study Funded by Department of Defense**

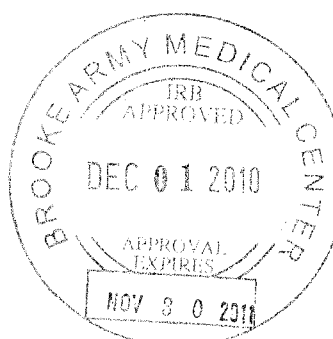
**We are asking you to volunteer to take part in a research study at the Carl R. Darnall Army Medical Center. It is important that you read and understand the information on this form. If you choose not to participate in this research study, your decision will not affect your eligibility for care or any other benefits to which you are entitled.**

**DESCRIPTION/PURPOSE OF RESEARCH:**

You are being asked to consider participation in this research study. The purpose of this study is to determine whether the medication fluoxetine, often used to treat depression, is an effective treatment for posttraumatic stress disorder (PTSD) and associated conditions in soldiers with recent war-zone exposure, as well as determine whether any response to fluoxetine is related to the degree of trauma exposure, the severity of PTSD symptoms, resistance to psychological trauma, adequacy of social supports (family, extra-military and military), the degree of post-deployment stressors and life problems, or the degree of any loss of memory. Many soldiers exposed to war-zone stress do not appear to have subsequent problems, however, as many as 20% (or one in five) will develop significant mental health problems because of their war exposure. The fact that such a significant number of soldiers have difficulty adapting to life after war exposure suggests that we need to have well-defined, affordable treatments that are effective. Currently, recommendations for medications to manage PTSD focus on the use of commonly prescribed antidepressants such as fluoxetine. Despite this recommendation by the Department of Defense (DoD)/Veterans Administration (VA) Clinical Practice Guidelines, there have not been any studies evaluating the effectiveness of these medications in patients that have recently been exposed to war-zone stressors. In fact, studies in Vietnam-Era veterans have shown limited effectiveness of these medications for PTSD. Also, there is very limited information available to understand the factors that influence whether a particular soldier will respond to treatment with these antidepressants. The procedures of this study will help identify which individuals with PTSD are likely to benefit from these medications.

This study will enroll approximately 300 subjects at the Carl R. Darnall Army Medical Center, over a period of three years. During your participation in this study, you will be asked to make approximately 11 one to two hour outpatient visits with Dr. Paul Hicks or other supporting staff at the Resilience and Restoration Center of the Carl R. Darnall Army Medical Center. This study involves the investigational (research) use of a drug called fluoxetine (the generic equivalent of Prozac). The Food & Drug Administration (FDA) has not yet approved this drug for treating PTSD.

*Revised June 2010*



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However, the FDA has not objected to its use to study its safety and effectiveness. The safety of fluoxetine (Prozac) in humans has been tested in prior research studies. Fluoxetine has been prescribed to millions of patients experiencing depression.

**INCLUSION AND EXCLUSION CRITERIA:**

To qualify for this study you must:

1. Be a veteran of the Operation Enduring Freedom/Operation Iraqi Freedom war campaigns with trauma exposure sufficient to qualify for a diagnosis of PTSD.
2. Meet criteria for a diagnosis of PTSD as determined by a standard questionnaire of symptoms, and have a minimum score on that questionnaire.
3. If you are female, you must have a negative serum pregnancy test and agree not to become pregnant for the duration of the study.

You will not be allowed to participate in this study if:

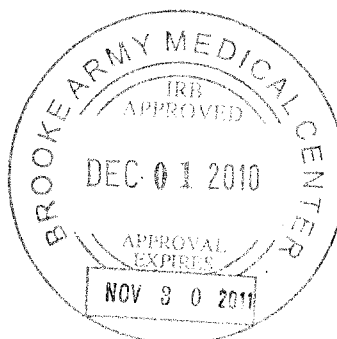
1. It is known that you are not able to tolerate fluoxetine.
2. It is known that you do not respond to fluoxetine at 60 mg daily.
3. You have a history of a significant mental disorder other than PTSD.
4. You have a significant history of suicidal or homicidal behavior/thoughts.
5. You have a history of dependence on any substances in the past 6 months.
6. You have a serious general medical condition that would prevent you from completing the study.
7. You have been using medications for depression or other mental health conditions except for zolpidem (Ambien) for the two weeks prior to beginning the study.
8. You are female and are found to be pregnant.
9. You have participated in another research drug trial within 30 days of enrollment.

**PROCEDURES:**

If you volunteer to participate in this study, we will ask you to do the following things:

1. If you are a qualified candidate and you agree to take part, the doctor or research staff will obtain your written informed consent to participate in this study. If you do participate, you must agree to carefully follow all the instructions that you are given.
2. Your medical history will be obtained and you will be physically examined by a physician associated with the study. For your own safety, it is your responsibility to tell the doctor all of your past and present diseases, allergies and medical conditions that you are aware of and all drugs and medications that you currently take.
3. Your height, weight, and blood pressure will be recorded.
4. A tablespoon (15 ml) of blood will be obtained at the first visit and at the sixth visit to estimate the degree of effect fluoxetine is producing on your brain chemistry.

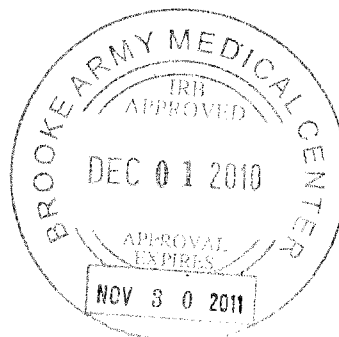
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5. Since this research may have bad effects on an unborn child and should not be performed during pregnancy, it is necessary that a pregnancy test be done first. If you are female a serum pregnancy test will be performed. To your knowledge, you are not pregnant at the present time. You also agree to avoid becoming pregnant (use contraceptives, take precautions against becoming pregnant, etc.) during this study.
6. As a participant, you will be asked to participate in two phases of this study. In the first phase, you will be randomly assigned to one of two treatments. Randomization is a process like flipping a coin and means you will have an equal chance of being assigned to either of the treatments. One of the two treatments will require you to take the study medication, fluoxetine (150 subjects), in increasing doses from 20 to 60 mg daily for a 12-week period. A second group will be assigned to receive placebo (150 subjects). A placebo is an inactive, harmless substance, like a sugar pill, that looks like the other study medications. You will have a one in two chance of being in the placebo group. The first phase of this study is a double-blind study, which means that neither you nor your providers will know whether you are receiving the study medication or a placebo. In the event of an emergency, however, there is a way to determine which you are receiving. **All subjects will continue to receive psychological treatments from their providers in the Resilience and Restoration Center at the Carl R. Darnall Army Medical Center throughout the study.**
7. In the second phase of this study you will be given fluoxetine in increasing doses, as needed, up to 80 mg daily for an additional 20 weeks. If you do not have significant improvement (greater than 50%) after being given 80 mg daily of fluoxetine for 4 weeks, then you will be assigned to also receive either bupropion SR (generic equivalent of Wellbutrin at 150 mg daily) or buspirone (generic equivalent of Buspar at up to 40 mg daily) for the remainder of the 20-week period in an attempt to improve your response to fluoxetine.
8. If you have trouble sleeping, you may be given a prescription for zolpidem (generic equivalent of Ambien).
9. The total participation time, including both phases of the study, will be 8 months duration.
10. The use of other prescription or over-the-counter medicines will not be allowed without your study doctor's approval. You will need to take part in regular outpatient visits while taking the study medication and must tell the doctor of any effects that you experience. During the study you should continue your normal dietary habits and vitamin intake. The use of tobacco will also be allowed during the study.

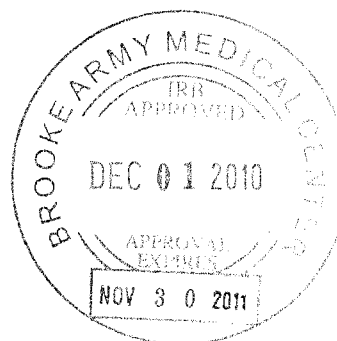
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11. You will be asked to complete questionnaires and answer questions about your symptoms and feelings at the beginning of the study and also at weeks 2, 4, 6, 8, 12, 16, 20, 24, 28 and 32. The tests will normally be completed in about 30-45 minutes. The testing will take longer (up to 2 1/2 hours long) before the start of the 1<sup>st</sup>, after the 12<sup>th</sup> week of treatment, and after the 32<sup>nd</sup> week. Approximately 25% (one-fourth) of the interviews will have audio recordings made so that reliability of the questionnaire measurements can be assessed. After reliability measurements are completed, the audiotapes will be destroyed. The questionnaires will require you to answer questions about:
- Your demographic information (e.g., age, race, education, etc.) and military service (e.g., rank, the number of years in the Service, etc.)
  - Any trauma you have experienced during your life
  - The amount of your combat exposure
  - Your symptoms and feelings, including anxiety, depression and PTSD symptoms
  - The stress and adversity your family has experienced since your deployment
  - The quality of your family relationships and social supports
  - The quality of your peer and leader supports
  - The quality of your physical health, activities of daily living, and overall life satisfaction
  - Your ability to withstand stressful events
  - Your memory, attention, and ability to use language
  - Whether there are any bad side effects to your study medications
  - Which medications you are taking
  - Your current use of alcoholic beverages
  - Your guess as to which treatment you are receiving
  - Your treatment expectations
12. Study personnel will also regularly assess your response to treatment and will ask detailed questions about the treatment effects and side effects. If your condition gets worse, the study medication may be stopped and you will be given other medication instead. If your condition improves you must still return for further visits until the study has finished.
13. If you need a procedure requiring additional informed consent, a separate consent form will be given to you before that procedure.
14. We will obtain information from your medical records concerning laboratory test results, medical diagnoses, pharmacy records, clinic and hospital visits, and any procedures performed.
15. Your name will not be mentioned in research publications that result from this study.
16. We cannot guarantee that you will be able to continue receiving fluoxetine after this study is over, but fluoxetine may be available through your family doctor.

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**RISKS, STRESS OR DISCOMFORT:**

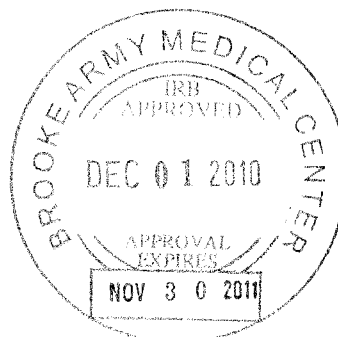
The potential side effects associated with the administration of fluoxetine include:

- nausea
- diarrhea
- restlessness
- headache
- sleeplessness
- inability to perform sexually (e.g. impotence, inability to have an orgasm, decreased sex drive)
- drowsiness
- tremors (shaking).
- If you receive placebo there may be less benefit and therefore the symptoms of PTSD may be present for a longer time
- In May 2007 the FDA approved the following additional information about the use of all antidepressants. Depression and other serious mental illnesses are the most important causes of suicidal thoughts and actions. Antidepressant medicines may increase suicidal thoughts or actions in some teenagers and young adults when the medicine is first started. Patients of all ages who are started on antidepressant therapy should be monitored appropriately and observed closely for clinical worsening, suicidality, or unusual changes in behavior. Families and caregivers should be advised of the need for close observation and communication with the prescriber. You may wish to advise your family and/or caregiver of your involvement in this study.

Zolpidem may cause:

- drowsiness, the intended benefit
- diarrhea
- nausea
- dry mouth
- muscle aches
- dizziness
- headaches
- confusion
- depression

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Buspirone may cause:

- nausea
- dizziness
- headache
- blurred vision
- agitation

Bupropion SR may cause:

- elevated blood pressure (hypertension)
- increased heart rate (tachycardia)
- rash
- sweating
- constipation
- nausea
- dry mouth
- confusion
- dizziness
- insomnia
- hostility
- tremor
- seizures (convulsions)

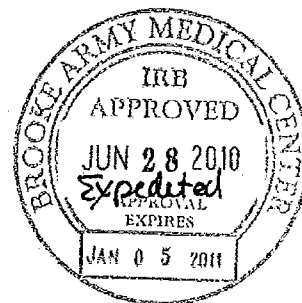
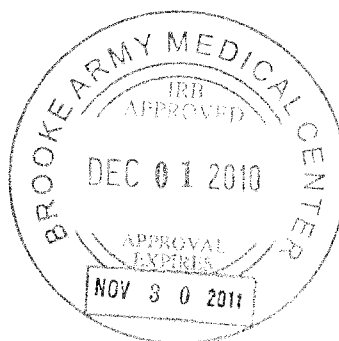
Other side effects may occur, some of which are not known and cannot be predicted. If you follow instructions and help the staff perform the appropriate examinations and laboratory tests, the chance of these unwanted side effects happening can be kept to a minimum. If side effects occur, you should contact the staff so that appropriate step to reduce them can be taken.

Some clients may experience some disruption of daily activities due to scheduling of the evaluation sessions. Also, answering questions that evoke painful memories will likely be uncomfortable for many subjects. Although you are free to decline to answer any questions you find objectionable, it is important for the purpose of this study that you try to answer all questions.

Pain, bruising, and rarely, fainting or infection may occur when blood is drawn on the first and sixth visits.

Consented participants, under the supervision of the study's psychiatrist(s), must discontinue any current psychotropic medication(s) prior to randomization in the study and may experience: worsened memory, increased depression, anxiety, or suicidal thoughts. Other side effects may occur

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during this period, some of which are not known and cannot be predicted. Side effects encountered will vary depending on the medication, dosage, diagnosis the medication is prescribed for, length of time it has been taken, characteristics (physical and mental) of the individual, etc. You are expected to keep the research staff informed of any and all effects/experiences you encounter during the medication discontinuation phase.

It is possible that the study medication may not be effective and that your condition may worsen. If, in the opinion of your study doctor, there are any problems caused by the study medication that make it unwise for you to continue taking it, you will be withdrawn from the study and appropriately treated by your doctor.

If you are a FEMALE OF CHILD BEARING POTENTIAL wishing to volunteer for this project, you must understand that fluoxetine, bupropion SR, zolpidem or buspirone might be harmful to (1) an unborn child if you are pregnant; or (2) an infant if you are breast-feeding. Studies evaluating the capability of the medication under investigation to produce birth defects in an unborn child have not been conducted. Therefore, you must not be pregnant during the study and will be required to take a pregnancy test before you participate in this study. You must also agree to take precautions to prevent pregnancy during the course of this study due to the possible severe harm the drug/procedure may cause your unborn child. The only completely reliable methods of birth control are total abstinence or surgical removal of the uterus. Other methods, such as the use of condoms, a diaphragm or cervical cap, birth control pills, IUD, or sperm killing products may not be totally effective in preventing pregnancy. Also, you must not breast-feed and participate in this study.

If you become pregnant or feel you might be pregnant, contact your provider and the study investigator listed in the Voluntary Participation section.

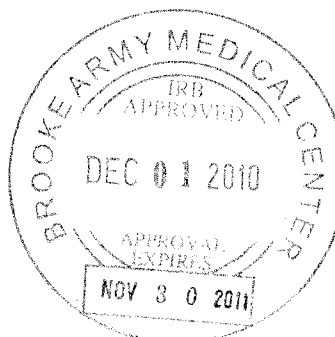
You will be kept informed of any significant new findings occurring during the course of the research that may influence your willingness to continue to participate in the study.

If you have any questions regarding the research, your participation, or suspect any research-related illness or injury, contact: **Dr. Michael Adams** at (254) 780-6420 or **Dr. Paul B. Hicks** at (254) 743-2643. After hours you may contact Dr. Paul B. Hicks, at (254) 760-8309.

**BENEFITS:**

The investigators have designed this study to learn if the new treatment is as good as or better than or worse than the most commonly accepted treatments. However, there is no guarantee or promise that you will receive any benefit from this study. The possible benefit of your participation in this study is that subjects are likely to receive some symptomatic improvement with the combination of psychological and pharmacological interventions offered in this study. If response is experienced,

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**Predictors of Treatment Response to Fluoxetine in PTSD Following a Recent History of War  
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the subject will have symptomatic improvement and will likely be able to better adapt to current stressors in their life.

There is no guarantee you will receive any benefit from this study other than knowing that the information may help future patients.

**PAYMENT (COMPENSATION):**

You will be paid \$50 for each blood draw for a maximum of \$100 for two blood draws.

**ALTERNATIVES TO PARTICIPATION:**

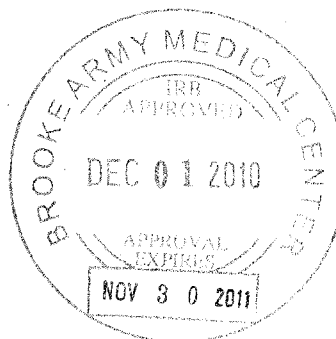
Participation in this study is entirely voluntary. **You may refuse to participate or may withdraw from the study at any time without penalty or loss of benefits to which you are otherwise entitled.** If you decide to withdraw from the research study, notify the staff and/or study doctor of your intention to do so. The study doctor may stop your participation if it is determined to be in your best interest or if you fail to follow the directions of the study doctor.

You do not have to participate in this study to receive treatment for your condition. The medication involved in this study may also be available through your family doctor without the need for you to volunteer to participate in this study. Other drugs are available as alternatives to the drugs being tested in this study. These alternative medications include sertraline (Zoloft®), citalopram (Celexa® or Lexapro®), which are approved for the treatment of PTSD.

**RESEARCH RESULTS**

1. During the course of the study, you will be informed of any significant new findings (either good or bad), such as changes in the risks or benefits resulting from participation in the research or new alternatives to participation that might cause you to change your mind about continuing in the study. If new information is provided to you, your consent to continue participating in this study will be re-obtained.
2. All questionnaires and study materials will remain in the possession of the investigators at the Carl R. Darnall Army Medical Center. Only the investigators and their research associates will have access to these materials. They will be stored in a secured, locked location for three years after the completion of the study. All questionnaires and all study materials will remain in the possession of the investigators at the Carl R. Darnall Army Medical Center in building 36009 for a minimum of five years after the completion of the study. They will be stored in a secured and locked cabinet, accessible only by the Overall Principal Investigator, Site Principal Investigator, Research Psychiatrist, and two Research Associates, all of whom will have a key. All study materials, questionnaires, notes, samples, and audiotapes, will be coded prior to usage and the key to the code will be kept by the pharmacy and research personnel in a locked drawer.

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Data will be securely stored in a de-identified manner. Biological samples will be coded at the time the sample is drawn and the de-identified samples will be transported to the CTVHCS lab for analysis and disposal. De-identified electronic media will be shipped via an established nationwide delivery company (e.g.: FedEx) to the Co-Principal Investigator at the National Center for PTSD, VA Boston Health Care System. Five years after closure of the study, any and all paper AND electronic documentation containing confidential, personally identifiable information, protected health information, and any other sensitive information will be disposed/destroyed according to current VA regulations at the time of disposal/destruction of documentation.

3. If results of this study are reported in medical journals or at meetings, you will not be identified by name, by recognizable photograph, or by any other means without your specific consent. Your medical records will be maintained according to Department of Defense (DoD) requirements.

**CONFIDENTIALITY OF RECORDS OF STUDY PARTICIPATION:**

Records of your participation in this study may only be disclosed in accordance with federal law, including the Federal Privacy Act, 5 U.S.C.552a, and its implementing regulations. DD Form 2005, Privacy Act Statement - Military Health Records, contains the Privacy Act Statement for the records. Your records may be reviewed by the U.S. Food & Drug Administration (FDA), other U.S. government agencies, the Brooke Army Medical Center Institutional Review Board, representatives of the US Army Medical Research and Materiel Command (USAMRMC), the Central Texas Veterans Health Care System (CTVHCS) Institutional Review Board. As a result, they may see your name; but they are bound by rules of confidentiality not to reveal your identity to others. Complete confidentiality cannot be promised, particularly for military personnel, because information regarding your health may be required to be reported to appropriate medical or command authorities.

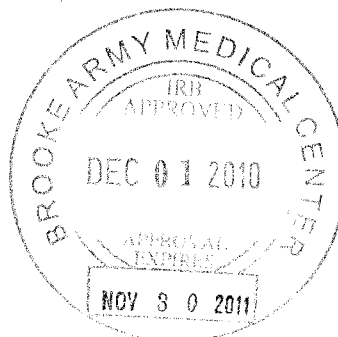
Confidentiality may be broken should you tell us you have thoughts of suicide, hurt/kill someone else, or any instances of current abuse of children, elders, or persons with disabilities.

By signing this consent document, you give your permission for information gained from your participation in this study to be published in medical literature, discussed for educational purposes, and used generally to further medical science. You will not be personally identified; all information will be presented as anonymous data.

**ENTITLEMENT TO CARE:**

In the event of injury resulting from this study, the extent of medical care provided is limited and will be within the scope authorized for Department of Defense (DoD) health care beneficiaries.

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**BROOKE ARMY MEDICAL CENTER/CARL R. DARNALL ARMY MEDICAL CENTER  
INFORMED CONSENT DOCUMENT**

**Predictors of Treatment Response to Fluoxetine in PTSD Following a Recent History of War  
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Your entitlement to medical and dental care and/or compensation in the event of injury is governed by federal laws and regulations, and if you have questions about your rights as a research subject or if you believe you have received a research-related injury, you may contact the Brooke Army Medical Center Protocol Coordinator at (210) 916-2598 or the Brooke Army Medical Center Judge Advocate General at (210) 808-4075 or the Carl R. Darnall Army Medical Center, Judge Advocate General, (254) 286-7339.

**SPECIAL INFORMATION:**

1. You are not required to take part in this study: your participation is entirely voluntary.
2. You can refuse to participate now or you can withdraw from the study at any time after giving your consent. This will not interfere with your regular medical treatment, if you are a patient.
3. There will be no costs to you for any of the treatment or testing done as part of this research study.
4. If you have questions about your rights as a research participant, you may contact **Dr. Michael Adams** at (254) 780-6420.
5. If you are a patient, this consent form will be placed in your medical record and a copy will be kept in the research office.

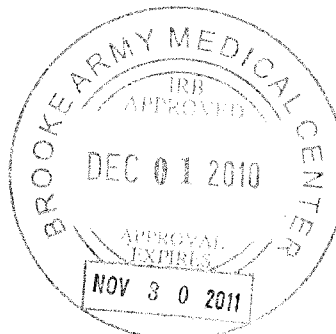
**VOLUNTARY PARTICIPATION:**

The decision to participate in this study is completely voluntary on your part. No one has coerced or intimidated you into participating in this project. You are participating because you want to. The Principal Investigator or one of his associates has adequately answered any and all questions you have about this study, your participation, and the procedures involved. If significant new findings develop during the course of this study that may relate to your decision to continue participation you will be informed.

You may withdraw this consent at any time and discontinue further participation in this study without affecting your eligibility for care or any other benefits to which you are entitled. Should you choose to withdraw, you must contact Dr. Paul Hicks or a member of the study staff at the following number (254) 743-2643 or **Dr. Michael Adams** at (254) 780-6420. You will be asked to complete end of study procedures. There are no consequences if you do not complete these procedures. Your condition will continue to be treated in accordance with acceptable standards of medical treatment. If you withdraw your consent, researchers may only use and disclose the information already collected for this study and, your information may still be used and disclosed should you have a bad effect.

The investigator of this study may terminate your participation in this study at any time if he/she feels this to be in your best interest. If you become ill during the research, you may have to drop out,

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Zone Stress Exposure**

even if you would like to continue. The investigator will make the decision and let you know if it is not possible for you to continue. The decision may be made either to protect your health and safety, or because it is part of the research plan that people who develop certain conditions may not continue to participate.

**CONTACT INFORMATION:**

**Site Principal Investigator (PI)**

The Site Principal Investigator or a member of the research staff will be available to answer any questions concerning procedures throughout this study.

Site Principal Investigator: **Dr. Michael Adams** at (254) 780-6420

In addition, the Principal Investigator will also be available to answer questions concerning procedures throughout this study.

Principal Investigator: **Dr. Paul B. Hicks** at (254) 743-2643

You have read the information provided above. You have been given an opportunity to ask questions and all of your questions have been answered to your satisfaction. You have been given a copy of this form. You agree to participate in this study on a voluntary basis. All oral and written information and discussions about this study have been in English, a language in which you are fluent.

A copy of this signed and dated form will be given to you.

May we contact you by: [ phone YES NO ] [ text message YES NO ] [ email YES NO ]

\_\_\_\_\_  
Volunteer's Signature

\_\_\_\_\_  
Phone #

\_\_\_\_\_  
Date

\_\_\_\_\_  
Volunteer's Printed Name

\_\_\_\_\_  
Date of Birth

\_\_\_\_\_  
Volunteer's Address (street, city, state & zip code)

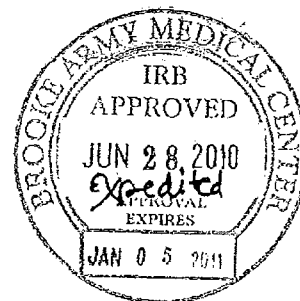
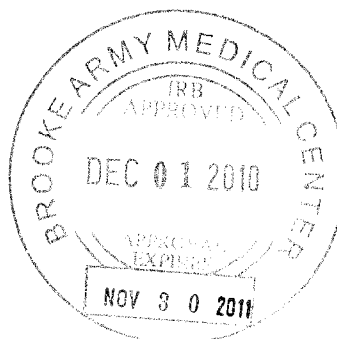
\_\_\_\_\_  
Advising Investigator's Signature

\_\_\_\_\_  
Date

\_\_\_\_\_  
Phone Number

*(can only be signed by an investigator whose name is listed in the protocol)*

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***Predictors of Treatment Response to Fluoxetine in PTSD Following a Recent History of War Zone Stress Exposure*** 1

**BROOKE ARMY MEDICAL CENTER/CARL R. DARNALL ARMY MEDICAL CENTER  
AUTHORIZATION TO USE AND DISCLOSE PROTECTED HEALTH INFORMATION  
FOR RESEARCH**

**(APHI Template Version 3, February 04)**

You are being asked for permission to use or disclose your protected health information for research purposes in the research study entitled "*Predictors of Treatment Response to Fluoxetine in PTSD Following a Recent History of War Zone Stress Exposure*".

The Health Insurance Portability & Accountability Act of 1996, Public Law 104-109 (also known as HIPAA), establishes privacy standards to protect your health information. This law requires the researchers to obtain your authorization (by signing this form) before they use or disclose your protected health information for research purposes in the study listed above.

**Your protected health information that may be used and disclosed in this study includes:**

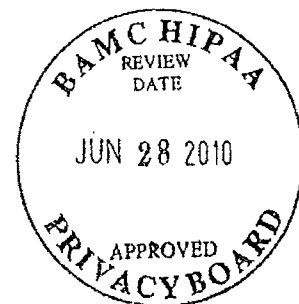
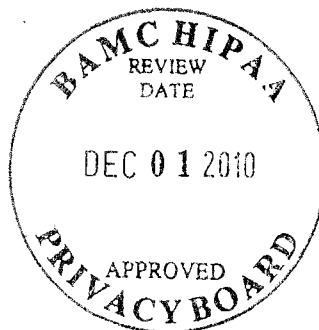
- Demographic information (e.g., age, race, education, etc.) and military service (e.g., rank, the number of years in the Service, etc.)
- Medical History/Surgical History
- Laboratory Results
- Responses to questionnaires
- Frequency, duration, content, and type of therapy treatment sessions with your current Usual Care Clinician (therapist)

**Your protected health information will be used for:**

The purpose of this study is to determine whether the medication fluoxetine, often used to treat depression, is an effective treatment for posttraumatic stress disorder (PTSD) and associated conditions in soldiers with recent war-zone exposure, as well as determine whether any response to fluoxetine is related to the degree of trauma exposure, the severity of PTSD symptoms, resistance to psychological trauma, adequacy of social supports (family, extra-military and military), the degree of post-deployment stressors and life problems, or the degree of any loss of memory.

The disclosure of your protected health information is necessary in order to be able to conduct the research project described. Records of your participation in this study may only be disclosed in accordance with state and federal law, including the Privacy Act (5 U.S.C. 552a) and the Health Insurance Portability and Accountability Act of 1996 and its implementing regulations (45 CFR 160 & 164). Note: Protected health information of military service members may be used or disclosed for activities deemed necessary by appropriate military command authorities to ensure the proper execution of the military mission.

By signing this authorization, you give your permission for information gained from your participation in this study to be published in medical literature, discussed for educational purposes, and used generally to further medical science. You will not be personally identified; all information will be presented as anonymous data.



***Predictors of Treatment Response to Fluoxetine in PTSD Following a Recent History of War Zone Stress Exposure*** 2

**The Principal Investigator may use and share your health information with:**

- The Central Texas Veterans Health Care System Institutional Review Board and the Brooke Army Medical Center/Carl R. Darnall Army Medical Center Institutional Review Board
- State and Federal Government representatives, when required by law
- Brooke Army Medical Center/Carl R. Darnall Army Medical Center Department of Defense representatives
- Representatives of the US Army Medical Research and Materiel Command (USAMRMC)
- Other collaborating investigators:
  - Paul B. Hicks, M.D., Ph.D.  
Central Texas Veterans Health Care System
  - Brett Litz, Ph.D.  
VA Boston Health Care System
  - Peggy Pazzaglia, M.D.  
Central Texas Veterans Health Care System, Psychiatrist
  - Leah M. Blackburn, M.A., L.P.C.  
Central Texas Veterans Research Foundation, Research Coordinator
  - John Reeve, Ph.D., L.P.C.-Intern  
Central Texas Veterans Research Foundation, Research Coordinator
  - Kamau Richard, M.S., L.P.C. Intern (effective until 30 June 2010)  
Central Texas Veterans Research Foundation, Research Coordinator

The researchers and those listed above agree to protect your health information by using and disclosing it only as permitted by you in this Authorization and as directed by state and federal law.

You need to be aware that some parties receiving your protected health information may not have the same obligations to protect your protected health information and may re-disclose your protected health information to parties not named here. If your protected health information is re-disclosed, it may no longer be protected by state or federal privacy laws.

**You do not have to sign this Authorization. If you decide not to sign the Authorization:**

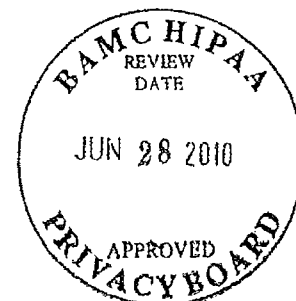
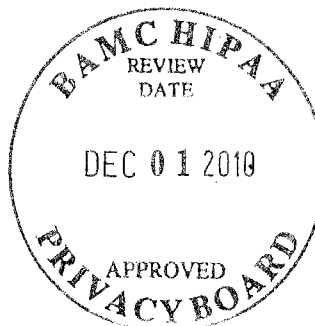
- It will not affect your treatment, payment or enrollment in any health plans or affect your eligibility for benefits.
- You may not be allowed to participate in the research study.

**After signing the Authorization, you can change your mind and:**

- Notify the researcher that you have withdrawn your permission to disclose or use your protected health information (revoke the Authorization).

If you revoke the Authorization, you will send a written letter to:

Michael L. Adams, Ph.D., LTC Ret.  
Carl R. Darnall Army Medical Center-TBI Clinic  
Box 16  
Building 36000 Darnall Loop  
Ft. Hood, TX 76544



*Predictors of Treatment Response to Fluoxetine in PTSD Following a Recent History of War Zone Stress Exposure* 3

to inform him of your decision.

- If you revoke this Authorization, researchers may only use and disclose the protected health information already collected for this research study.
- If you revoke this Authorization your protected health information may still be used and disclosed should you have an adverse event (a bad effect).
- If you withdraw the Authorization, you may not be allowed to continue to participate in the study.

During your participation in this study, you will not be able to access your research records. This is done to ensure the study results are reliable. After the completion of the study, you have the right to see or copy your research records related to the study listed above. A Request for Access must be made in writing to:

Michael L. Adams, Ph.D., LTC, Ret.  
Carl R. Darnall Army Medical Center-TBI Clinic  
Box 16  
Building 36000 Darnall Loop  
Ft. Hood, TX 76544

If you have not already received a copy of the brochure entitled "Military Health System Notice of Privacy Practices," you may request one. DD Form 2005, Privacy Act Statement - Military Health Records (located on your medical records jacket), contains the Privacy Act Statement for the records. If you have any questions or concerns about your privacy rights, you should contact the Brooke Army Medical Center Privacy Officer at phone number (210) 916-1029 or Central Texas Veterans Health Care System Privacy Officer at 1-800-423-2111, ext 42055.

This Authorization does not have an expiration date.

You are the subject. You have read this information, and will receive a copy of this form after it is signed.

May we contact you by: [ phone YES NO ] [ text message YES NO ] [ email YES NO ]

I consent to the release of the above stated information from \_\_\_\_\_  
my off-post Usual Care Clinician (therapist). (print therapist name)

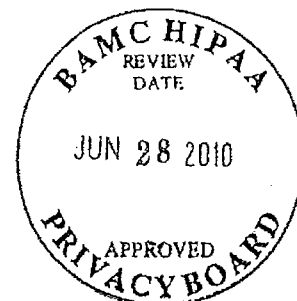
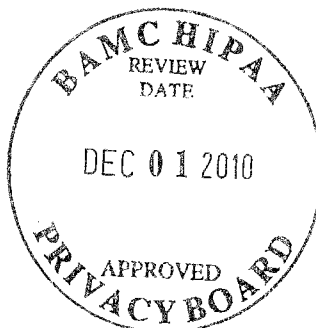
\_\_\_\_\_  
Volunteer's Signature

\_\_\_\_\_  
Date

\_\_\_\_\_  
Volunteer's Printed Name

\_\_\_\_\_  
Signature of Witness

\_\_\_\_\_  
Date





**Appendix B: CTVHCS IRB Continuing Review Approval Letter, Approved Informed Consent Document, and HIPAA Consent Form**

Institutional Review Board (IRB)  
Temple VA Medical Center

Temple, TX

IRB APPROVAL - Amendment

Date: May 13, 2011  
From: John W. Klocek, Ph.D.  
Investigator: Paul B. Hicks, M.D., Ph.D.  
Protocol: Predictors of Treatment Response to Fluoxetine in PTSD Following A  
Recent History of War Zone Stress Exposure  
ID: 00308 Prom#: 0016 Protocol#: N/A

The following items were reviewed and approved at the 12/08/2010 meeting, contingent upon stipulations in each item marked with an asterisk (\*):

- Advertisement (Received with 11/1/10 amendment)
- Amendment - Protocol Amendment to add VA as site (11/01/2010)
- \* Consent Form - clean copy and changes tracked (2, Nov 2010)
- Memo from PI re IRB req'd changes/clarification (01/05/2011)
- Memo with additional changes (11/18/2010)
- Protocol, clean copy and changes tracked (11/18/2010; 7)
- Data Transfer Agreement (11/03/2010)
- Information for Laboratory Staff
- Instruction for Research Participant
- Lab signature/blood draw payment
- VA Fm 10-3203, Consent for Use of Picture or Voice (John Reeve)
- VA Fm 10-3203, Consent for Use of Picture or Voice (Leah Blackburn)
- VA Fm 10-3203, Consent for Use of Picture or Voice (Paul Hicks)
- VA Fm 10-3203, Consent for Use of Picture or Voice (Peggy Pazzaglia)
- Medical Alert / Emergency Contact cards (Received with 01/05/11 documents)
- Checklist for participants (Received with 11/1/10 amendment)
- Revocation of HIPAA (Received with 11/1/10 amendment)
- Schedule of Appointments (Received with 11/1/10 amendment)
- Questionnaire / Survey - PCL 5
- Support Letters - Chief P&LMS Spt Memo (01/31/2011)
- Support Letters - Chief Pharmacy Svc Support Memo (01/11/2011)
- Request to Review Research Proposal/Project (11/18/2010; Nov 2010)

Consent Form - clean copy and changes tracked (2, Nov 2010) was returned to you with stipulations. The following revised items incorporate the stipulations and are now approved:

- Consent Form - clean copy and changes tracked (3, Jan 2011)


The following Institutional Review Board (IRB) members were not in attendance and did not vote: Paul B. Hicks, M.D., Ph.D.

The protocol was determined to have the following level of risk: Moderate

The protocol was determined to have the following level of benefit to participants:  
Prospect for direct benefit to participants

Corrected memorandum: Correction made to the IRB memorandum dated April 19, 2011, to reflect the date of receipt for the Medical Alert/Emergency Contact card; to revise number 3, below to reflect the correct version and date of the VA Research Consent Form; and to list all items received with the November 1, 2010 protocol amendment.

1. The IRB members reviewed the above revisions at the December 8, 2010, meeting. The revisions consisted of changes and/or clarification of items that were requested by the IRB in the December 16, 2010, IRB memorandum. The revisions consisted of a request to add the Central Texas Veterans Health Care System as a site for the study.
2. The amendment was approved contingent upon revisions to the informed consent document (ICD) and the Health Insurance Portability and Accountability Act (HIPAA) form, submission of the Participant Laboratory Instruction Form and service support memorandums for the Chiefs, Pharmacy and Laboratory Services. These documents were revised as requested.
3. All stipulations have been approved. The VA Research Consent Form, VA Form 10-1086, version 4, dated Mar 2011, will be stamped with the continuing review documents.
4. If additional information is needed, please call Ms. Thomas, Program Specialist, at extension 41974.

  
John W. Klocek, Ph.D.  
CTVHCS, IRB Chair

0210 - included  
changed since word  
with 2/11

**Institutional Review Board (IRB)**  
**Temple VA Medical Center**  
Temple, TX

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**IRB APPROVAL - Amendment**

Date: April 19, 2011

From: John W. Klocek, Ph.D.

Investigator: Paul B. Hicks, M.D., Ph.D.

Protocol: Predictors of Treatment Response to Fluoxetine in PTSD Following A Recent History of War Zone Stress Exposure

ID: 00308 Prom#: 0016 Protocol#: N/A

The following items were reviewed and approved at the 12/08/2010 meeting, contingent upon stipulations in each item marked with an asterisk (\*):

- Amendment - Protocol Amendment to add VA as site (11/01/2010)
- \* Consent Form - clean copy and changes tracked (2, Nov 2010)
- Memo from PI re IRB req'd changes/clarification (01/05/2011)
- Memo with additional changes (11/18/2010)
- Protocol, clean copy and changes tracked (11/18/2010; 7)
- Data Transfer Agreement (11/03/2010)
- Information for Laboratory Staff
- Instruction for Research Participant
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- VA Fm 10-3203, Consent for Use of Picture or Voice (Paul Hicks)
- VA Fm 10-3203, Consent for Use of Picture or Voice (Peggy Pazzaglia)
- Support Letters - Chief P&LMS Spt Memo (01/31/2011)
- Support Letters - Chief Pharmacy Svc Support Memo (01/11/2011)
- Request to Review Research Proposal/Project (11/18/2010; Nov 2010)

Consent Form - clean copy and changes tracked (2, Nov 2010) was returned to you with stipulations. The following revised items incorporate the stipulations and are now approved:

- Consent Form - clean copy and changes tracked (3, Jan 2011)


The following Institutional Review Board (IRB) members were not in attendance and did not vote: Paul B. Hicks, M.D., Ph.D.

The protocol was determined to have the following level of risk:

Moderate

The protocol was determined to have the following level of benefit to participants:  
Prospect for direct benefit to participants

1. The IRB members reviewed the above revisions at the December 8, 2010, meeting. The revisions consisted of changes and/or clarification of items that were requested by the IRB in the December 16, 2010, IRB memorandum. The revisions consisted of a request to add the Central Texas Veterans Health Care System as a site for the study.
2. The amendment was approved contingent upon revisions to the informed consent document (ICD) and the Health Insurance Portability and Accountability Act (HIPAA) form, submission of the Participant Laboratory Instruction Form and service support memorandums for the Chiefs, Pharmacy and Laboratory Services. These documents were revised as requested.
3. All stipulations have been approved. The VA Research Consent Form, VA Form 10-1086, version 6, dated January 31, 2011, will be stamped with the continuing review documents.
4. If additional information is needed, please call Ms. Thomas, Program Specialist, at extension 41974.

  
John W. Kloczek, Ph.D.  
CTVHCS, IRB Chair

Subject Name: \_\_\_\_\_

Date: \_\_\_\_\_

Title of Study: *Predictors of Treatment Response to Fluoxetine in PTSD Following a Recent History of War Zone Stress Exposure*

Principal Investigator: Paul B. Hicks, MD, PhD

VAMC: CTVHCS

### DESCRIPTION OF RESEARCH BY INVESTIGATOR

1. Purpose of study and how long it will last:
2. Description of the study including procedures to be used:
3. Description of any procedures that may result in discomfort or inconvenience:
4. Expected risks of study:
5. Expected benefits of study:
6. Other treatment available:
7. Use of research results:
8. Special Circumstances:

The study you are being asked to volunteer to take part in involves research. This research study takes place at the Central Texas Veterans Health Care System (CTVHCS) for veterans and the Carl R. Darnall Army Medical Center for active duty soldiers. It is important that you read and understand the information on this form.

### PURPOSE

The purpose of this research is to determine whether the medication fluoxetine, often used to treat depression, is an effective treatment for posttraumatic stress disorder (PTSD) and associated conditions in soldiers and veterans with recent war-zone exposure, as well as determine whether any response to fluoxetine is related to the degree of trauma exposure, the severity of PTSD symptoms, resistance to psychological trauma, adequacy of social supports (family, extra-military and military), the degree of post-deployment stressors and life problems, or the degree of any loss of memory. Many of those exposed to war-zone stress do not appear to have subsequent problems, however, as many as 20% (or one in five) will develop significant mental health problems because of their war exposure. The fact that such significant numbers have difficulty adapting to life after war exposure suggests that we need to have well-defined, affordable treatments that are effective. Currently, recommendations for medications to manage PTSD focus on the use of commonly prescribed antidepressants such as fluoxetine. Despite this recommendation by the Department of Defense (DoD)/Veterans Administration (VA) Clinical Practice Guidelines, there have not been any studies evaluating the effectiveness of these medications in patients that have recently been exposed to war-zone stressors. In fact, studies in Vietnam-Era veterans have shown limited effectiveness of these medications for PTSD. Also, there is very limited information available to understand the factors that influence whether a particular soldier or veteran will respond to treatment with these antidepressants. The procedures of this study will help identify which individuals with PTSD are likely to benefit from these medications.

SUBJECT'S IDENTIFICATION (I.D. plate of give name - last, first, middle)



Approved 4/13/11 to 4/12/12

Subject Name: \_\_\_\_\_

Date: \_\_\_\_\_

Title of Study: *Predictors of Treatment Response to Fluoxetine in PTSD Following a Recent History of War Zone Stress Exposure*

Principal Investigator: Paul B. Hicks, MD, PhD

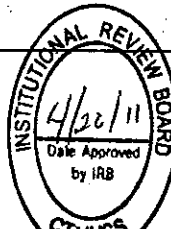
VAMC: CTVHCS

This research study is a multicenter research project which will study approximately 300 participants. This study will last approximately three years. During your participation in this study, you will be asked to make approximately 11 one to two hour outpatient visits with Dr. Paul Hicks or other supporting staff at Central Texas Veterans Health Care System. This study involves the investigational (research) use of a drug called fluoxetine (the generic equivalent of Prozac). The Food & Drug Administration (FDA) has not yet approved this drug for treating PTSD. However, the FDA has not objected to its use to study its safety and effectiveness. The safety of fluoxetine (Prozac) in humans has been tested in prior research studies. Fluoxetine has been prescribed to millions of patients experiencing depression.

### PROCEDURES

If you consent to participate in this research study, we will ask you to do the following things:

1. If you are a qualified candidate and you agree to take part, the doctor or research staff will obtain your written informed consent to participate in this study. If you do participate, you must agree to carefully follow all the instructions that you are given.
2. Your medical history will be obtained and you will be physically examined by a physician associated with the study. For your own safety, it is your responsibility to tell the doctor all of your past and present diseases, allergies, and medical conditions that you are aware of and all drugs and medications that you currently take.
3. Your height, weight, and blood pressure will be recorded.
4. A tablespoon (15 ml) of blood will be obtained at the first visit and at the sixth visit to estimate the degree of effect fluoxetine is producing on your brain chemistry.
5. Since this research may have bad effects on an unborn child and should not be done during pregnancy, it is necessary that a pregnancy test be done first. If you are female a blood pregnancy test will be performed. To your knowledge, you are not pregnant now. You also agree to avoid becoming pregnant (use contraceptives; take precautions against becoming pregnant, etc.) during this study.
6. As a participant, you will be asked to participate in two phases of this study. In the first phase, you will be randomly assigned to one of two treatments. Using a procedure like flipping a coin, you will have a 1 in 2 chance of receiving a sugar pill instead of fluoxetine. You have an equal chance of being assigned to either of the two treatments. One of the two treatments will require you to take the study medication, fluoxetine (150 subjects), in increasing doses from 20 to 60 mg daily for a 12-week period. A second group will be assigned to receive placebo (150 subjects). A placebo is an inactive, harmless substance, like a sugar pill, that looks like the other study medications. You will have a one in two chance of being in the placebo group.
7. The first phase of this study is a double-blind study, which means that neither you nor your providers will know whether you are receiving the study medication or a placebo. In the event of an emergency, however, there is a way to determine which you are receiving. All subjects will continue to receive psychological treatments from their providers in the Central Texas Veterans Health Care System throughout the study.
8. In the second phase of this study you will be given fluoxetine in increasing doses, as needed, up to 80 mg daily for an additional 20 weeks. If you do not have significant improvement (greater than 50%) after being given 80 mg daily of fluoxetine for 4 weeks, then you will be assigned to also receive either bupropion SR (generic equivalent of Wellbutrin at 150 mg daily) or buspirone (generic equivalent of Buspar at up to 40 mg daily) for the remainder of the 20-week period in an attempt to improve your response to fluoxetine.



Subject Name: \_\_\_\_\_

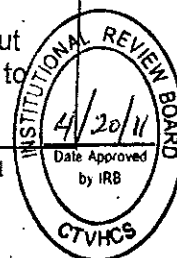
Date: \_\_\_\_\_

Title of Study: *Predictors of Treatment Response to Fluoxetine in PTSD Following a Recent History of War Zone Stress Exposure*

Principal Investigator: Paul B. Hicks, MD, PhD

VAMC: CTVHCS

9. If you have trouble sleeping, you may be given a prescription for zolpidem (generic equivalent of Ambien).
10. The total participation time, including both phases of the study, will be 8 months duration.
11. The use of other prescription or over-the-counter medicines will not be allowed without your study doctor's approval. You will need to take part in regular outpatient visits while taking the study medication and must tell the doctor of any effects that you experience. During the study you should continue your normal dietary habits and vitamin intake. The use of tobacco will also be allowed during the study.
12. You will be asked to complete questionnaires and answer questions about your symptoms and feelings at the beginning of the study and also at weeks 2, 4, 6, 8, 12, 16, 20, 24, 28 and 32. The tests will normally be completed in about 30-45 minutes. The testing will take longer (up to 2 1/2 hours long) before the start of the 1<sup>st</sup>, after the 12<sup>th</sup> week of treatment, and after the 32<sup>nd</sup> week. Approximately 25% (one-fourth) of the interviews will have audio recordings made so that reliability of the questionnaire measurements can be assessed. The questionnaires will require you to answer questions about:
  - Your demographic information (e.g., age, race, education, etc.) and military service (e.g., rank, the number of years in the Service, etc.)
  - Any trauma you have experienced during your life
  - The amount of your combat exposure
  - Your symptoms and feelings, including anxiety, depression and PTSD symptoms
  - The stress and adversity your family has experienced since your deployment
  - The quality of your family relationships and social supports
  - The quality of your peer and leader supports
  - The quality of your physical health, activities of daily living, and overall life satisfaction
  - Your ability to withstand stressful events
  - Your memory, attention, and ability to use language
  - Whether there are any bad side effects to your study medications
  - Which medications you are taking
  - Your current use of alcoholic beverages
  - Your guess as to which treatment you are receiving
  - Your treatment expectations
13. Study personnel will also regularly assess your response to treatment and will ask detailed questions about the treatment effects and side effects. If your condition gets worse, the study medication may be stopped and you will be given other medication instead. If your condition improves you must still return for further visits until the study has finished.
14. If the study physicians believe you will need any additional procedure(s) to maintain the standards of care given in psychiatry, and if those procedures require additional informed consent, a separate consent form will be given to you before that procedure.
15. We will obtain information from your medical records concerning laboratory test results, medical diagnoses, pharmacy records, clinic and hospital visits, and any procedures performed.
16. Your name will not be mentioned in research publications that result from this study.
17. You may withdraw this consent at any time and discontinue further participation in this study without affecting your eligibility for care or any other benefits to which you are entitled. Should you choose to withdraw, you must contact Dr. Paul Hicks or a member of the study staff at the following number





Subject Name: \_\_\_\_\_

Date: \_\_\_\_\_

Title of Study: Predictors of Treatment Response to Fluoxetine in PTSD Following a Recent History of War Zone Stress ExposurePrincipal Investigator: Paul B. Hicks, MD, PhD

VAMC: CTVHCS

(254) 760-8309. You will be asked to complete end of study procedures. There are no consequences if you do not complete these procedures. Your condition will continue to be treated in accordance with acceptable standards of medical treatment. If you withdraw your consent, researchers may only use and disclose the information already collected for this study and, your information may still be used and disclosed should you have a bad effect.

**DISCOMFORTS AND RISKS**

The potential side effects associated with the administration of the medications include:

Fluoxetine may cause:

- nausea
- diarrhea
- restlessness
- headache
- sleeplessness
- inability to perform sexually (e.g. impotence, inability to have an orgasm, decreased sex drive)
- drowsiness
- tremors (shaking).
- If you receive placebo there may be less benefit and therefore the symptoms of PTSD may be present for a longer time
- In May 2007 the FDA approved the following additional information about the use of all antidepressants. Depression and other serious mental illnesses are the most important causes of suicidal thoughts and actions. Antidepressant medicines may increase suicidal thoughts or actions in some teenagers and young adults when the medicine is first started. Patients of all ages who are started on antidepressant therapy should be monitored appropriately and observed closely for clinical worsening, suicidality, or unusual changes in behavior. Families and caregivers should be advised of the need for close observation and communication with the prescriber. You may wish to advise your family and/or caregiver of your involvement in this study.

Zolpidem may cause:

- drowsiness, the intended benefit
- diarrhea
- nausea
- dry mouth
- muscle aches
- dizziness
- headaches
- confusion
- depression



Subject Name: \_\_\_\_\_

Date: \_\_\_\_\_

Title of Study: Predictors of Treatment Response to Fluoxetine in PTSD Following a Recent History of War Zone Stress Exposure

Principal Investigator: Paul B. Hicks, MD, PhD

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Buspirone may cause:

- nausea
- dizziness
- headache
- blurred vision
- agitation

Bupropion SR may cause:

- elevated blood pressure (hypertension)
- increased heart rate (tachycardia)
- rash
- sweating
- constipation
- nausea
- dry mouth
- confusion
- dizziness
- insomnia
- hostility
- tremor
- seizures (convulsions)

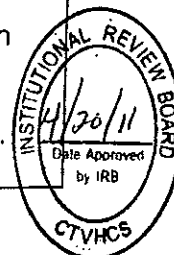
Other side effects may occur, some of which are not known and cannot be predicted. If you follow instructions and help the staff perform the appropriate examinations and laboratory tests, the chance of these unwanted side effects happening can be kept to a minimum. If side effects occur, you should contact the staff so that appropriate steps to reduce them can be taken.

Answering questions that evoke painful memories will likely be uncomfortable for many subjects. Although you are free to decline to answer any questions you find objectionable, it is important for the purpose of this study that you try to answer all questions.

Some clients may experience some disruption of daily activities due to scheduling of the evaluation sessions.

Pain, bruising, and rarely, fainting or infection may occur when blood is drawn on the first and sixth visits.

Consented participants, under the supervision of the study's psychiatrist(s), must discontinue any current psychotropic medication(s) prior to randomization in the study and may experience: worsened memory, increased depression, anxiety, or suicidal thoughts. Other side effects may occur during this period, some of which are not known and cannot be predicted. Side effects encountered will vary depending on the medication, dosage, diagnosis the medication is prescribed for, length of time it has been taken, characteristics (physical and mental) of the individual, etc. You are expected to keep the research staff informed of any and all effects/experiences you encounter during the medication discontinuation phase.



Subject Name: \_\_\_\_\_

Date: \_\_\_\_\_

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It is possible that the study medication may not be effective and that your condition may worsen. If, in the opinion of your study doctor, there are any problems caused by the study medication that make it unwise for you to continue taking it, you will be withdrawn from the study and appropriately treated by your doctor.

If you are a FEMALE OF CHILD BEARING POTENTIAL wishing to volunteer for this project, you must understand that fluoxetine, bupropion SR, zolpidem or buspirone might be harmful to (1) an unborn child if you are pregnant; or (2) an infant if you are breast-feeding. Studies evaluating the capability of the medication under investigation to produce birth defects in an unborn child have not been conducted. Therefore, you must not be pregnant during the study and will be required to take a pregnancy test before you participate in this study. You must also agree to take precautions to prevent pregnancy during the course of this study due to the possible severe harm the drug/procedure may cause your unborn child. The only completely reliable methods of birth control are total abstinence or surgical removal of the uterus. Other methods, such as the use of condoms, a diaphragm or cervical cap, birth control pills, IUD, or sperm killing products may not be totally effective in preventing pregnancy. Also, you must not breast-feed and participate in this study. If you are pregnant or become pregnant, the particular treatment/procedure may involve risks to the embryo or fetus, which are currently unforeseeable.

If you become pregnant or feel you might be pregnant, contact your provider and the study investigator listed in the Voluntary Participation section.

This particular treatment/procedure may involve risks to the participant, which are currently unforeseeable.

#### **BENEFITS**

The investigators have designed this study to learn if the new treatment is as good as or better than or worse than the most commonly accepted treatments. However, there is no guarantee or promise that you will receive any benefit from this study. The possible benefit of your participation in this study is that participants may receive some symptom improvement with the use of the offered study medicine(s). If response is experienced, you may have improvement of your symptoms and may be able to better adapt to current stressors in your life.

You may not personally be helped by taking part in this study, but your participation may lead to knowledge that will help others.

#### **OTHER TREATMENT AVAILABLE**

You do not have to participate in this study to receive treatment for your condition. The medication involved in this study may also be available through a VA doctor without the need for you to volunteer to participate in this study. Other drugs are available as alternatives to the drugs being tested in this study. These alternative medications include sertraline (Zoloft®), citalopram (Celexa® or Lexapro®), which are approved for the treatment of PTSD.

#### **RESEARCH RESULTS**

1. During the course of the study, a research psychiatrist will inform you of any significant new findings (either good or bad), such as changes in the risks or benefits resulting from participation in the.



Subject Name: \_\_\_\_\_

Date: \_\_\_\_\_

Title of Study: Predictors of Treatment Response to Fluoxetine in PTSD Following a Recent History of War Zone Stress Exposure

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research or new alternatives to participation that might cause you to change your mind about continuing in the study. If new information is provided to you, your consent to continue participating in this study will be re-obtained. A research psychiatrist will let you know of any important discoveries made during this study which may affect you, your condition, or your willingness to participate in this study.

2. All questionnaires and study materials obtained from veterans at the Central Texas Veterans Health Care System (CTVHCS) will remain in the possession of the principal investigator at CTVHCS. Only the investigator and his research staff will have access to these materials. Materials will be stored in the possession of the principal investigator at the CTVHCS, during and after the completion of the study, in a secured and locked cabinet, accessible only by the Overall Principal Investigator, Research Psychiatrist, and two Research Coordinators, all of whom may have a key. All study materials, questionnaires, notes, samples, and audio recordings, will be coded prior to usage and the key to the code will be kept by the pharmacy and research personnel in a locked cabinet or safe. Data will be securely stored in a manner, where only authorized members of the research team can determine to whom those data belong. Biological samples will be coded at the time the sample is drawn and the samples will be transported to the CTVHCS Research lab for analysis and disposal; research lab personnel are not able to match the code to a participant name. Electronic media will be shipped via an established nationwide delivery company to the Associate Investigator at the VA Boston Health Care System who will not be able to match the code to a participant name.
3. After closure of the study, any and all paper AND electronic documentation containing confidential, personally identifiable information, protected health information, and any other sensitive information will be disposed/destroyed according to current VA regulations at the time of disposal/destruction of documentation. Current requirements are that required records, including the investigator's research records; must be retained indefinitely until disposition instructions are approved by the National Archives and Records Administration and are published in VHA's Records Control Schedule (RCS 10-1).
4. If results of this study are reported in medical journals or at meetings, you will not be identified by name, by recognizable photograph, or by any other means without your specific consent. Your private information will be maintained according to this medical center's requirements.
5. Your medical and research records will be maintained according to this medical center's requirements. There is a possibility that the Office for Human Research Protections (OHRP), Food and Drug Administration (FDA), VA Office of Inspector General (OIG), Government Accounting Office (GAO), Veterans Health Administration (VHA), US Army Medical Research and Materiel Command (USAMRMC), other oversight agencies including the Office of Research Oversight (ORO), the Research Compliance Officer, Institutional Review Board members or other research staff may have access to your research and/or medical records or may inspect the records. Data will be analyzed by an Associate Investigator at the VA Boston Healthcare System. Every effort will be made to keep information about you both private and confidential. Codes (not your name and/or social security number) will be used for all reports generated, to help maintain your confidentiality.

### SPECIAL INFORMATION

1. If you experience an illness or injury as a direct result of the research procedures used in this clinical study while following all directions given by the research staff, then reasonable and necessary medical care will be given to you without charge. You should notify Dr. Paul B. Hicks as soon as you believe you have experienced any study related illness or injury at (254) 760-8309.



Subject Name: \_\_\_\_\_ Date: \_\_\_\_\_

Title of Study: *Predictors of Treatment Response to Fluoxetine in PTSD Following a Recent History of War Zone Stress Exposure*

Principal Investigator: Paul B. Hicks, MD, PhD VAMC: CTVHCS

For more information on medical treatment related to a study-related illness or injury, contact Dr. Hicks at (254) 760-8309.

The free medical care does not include care for any other illnesses or injuries that may happen while taking part in the clinical research study if it is determined that the illness and/or injury are not related to the study.

2. The decision to participate in this study is completely voluntary on your part. No one has coerced or intimidated you into participating in this project. You are participating because you want to. The Principal Investigator or one of his associates has adequately answered any and all questions you have about this study, your participation, and the procedures involved. If significant new findings develop during the course of this study that may relate to your decision to continue participation you will be informed. You are not required to take part in this study; your participation is entirely voluntary. You can refuse to participate now or you can withdraw from this study at any time after giving your consent. Refusal to participate will involve no penalty or loss of benefits to which you are otherwise entitled.
3. Veteran participants do not pay for treatment associated with participation in a VA research project except in accordance with federal law. There will be no costs to you for any of the treatment or testing done as part of this research study. Some veterans are required to pay co-payments for medical care and services provided by VA. These co-payment requirements will continue to apply to medical care and services provided by VA that are not part of this study.
4. VA must provide necessary medical treatment to a research subject injured by participation in a research project approved by a VA R&D Committee and conducted under the supervision of one or more VA employees. Except in limited circumstances, the necessary care must be provided in VA Medical facilities. Exceptions include: situations where VA facilities are not capable of furnishing the care or services required; and situations involving a non-veteran research subject. Under these circumstances, Directors *may* contract for such care.
5. In case there are medical problems, research related injuries, or questions, you may call Dr. Paul B. Hicks at (254) 760-8309. If any medical problems occur in connection with this study, the VA will provide emergency care.
6. There will be no costs to you for any of the treatment or testing done as part of this research study.

You will be paid \$50 for each blood draw for a maximum of \$100 for two blood draws. You will receive a blood draw kit, with an Instructions for Research Participants form enclosed, at the time of your initial and week 12 lab work. Blood will be drawn at the CTVHCS lab where, once the procedure is complete, the lab will sign and stamp the back of the Instructions for Research Participant form. You will return to the research area with the signed form to receive a \$50 payment (each blood draw receives a \$50 payment; there is no payment for a pregnancy test blood draw). When payment is made, the research personnel will have you sign the lab form as receiving payment and will date/sign the lab form as having paid you.

7. There is no promise that the medication you take during this study will be continued after the study is finished. If you are a veteran and can receive care at the VA, you may be able to receive the same drug after the study only if the CTVHCS pharmacy has the drug, and your physician decides that it is the best treatment for you.
8. The investigator of this study may terminate your participation in this study at any time if he feels this to be in your best interest. If you become ill during the research, you may have to drop out, even if



Subject Name: \_\_\_\_\_

Date: \_\_\_\_\_

Title of Study: Predictors of Treatment Response to Fluoxetine in PTSD Following a Recent History of War Zone Stress ExposurePrincipal Investigator: Paul B. Hicks, MD, PhD

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you would like to continue. The investigator will make the decision and let you know if it is not possible for you to continue. The decision may be made either to protect your health and safety, or because it is part of the research plan that people who develop certain conditions may not continue to participate.

9. As a research participant in this study, if you have a complaint about any issue regarding the study, or the research investigator; or, if you have questions about your rights as a research participant, you may contact Mariory D. Williams, Ph.D., R.N., Chairperson, Institutional Review Board at (254) 534-0418.
10. The clinical trial information will be entered into the clinical trial registry databank maintained by the National Institutes of Health/National Library of Medicine found at *ClinicalTrials.gov*.

**POTENTIAL CONFLICTS OF INTEREST**

1. The study is sponsored by the Department of Defense.
2. The sponsor provides a fixed payment to the Central Texas Veterans Research Foundation for performing the study.



Subject Name: \_\_\_\_\_

Date: \_\_\_\_\_

Title of Study: Predictors of Treatment Response to Fluoxetine in PTSD Following a Recent History of War Zone Stress Exposure

Principal Investigator: Paul B. Hicks, MD, PhD

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## AFFIRMATION FROM PARTICIPANT

RESEARCH PARTICIPANT'S RIGHTS: I have read or have had read to me all of the above. Dr. Paul B. Hicks, or his research staff, has explained the study to me and answered all of my questions. I have been told of the risks or discomforts and possible benefits of the study. I have been told of other choices of treatment available to me.

I understand that I do not have to take part in this study, and my refusal to participate will involve no penalty or loss of rights to which I am entitled. I may withdraw from this study at any time without penalty or loss of VA or other benefits to which I am entitled.

I understand my rights as a research participant. I understand what the study is about and how and why it is being done. I voluntarily consent to participate in this study. I know I will receive a signed copy of this consent form.

Research Participant's Signature \_\_\_\_\_

Date \_\_\_\_\_

Signature of Person Obtaining Consent \_\_\_\_\_

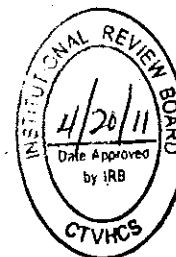
Date \_\_\_\_\_

THIS FORM IS NOT VALID UNLESS THE FOLLOWING BOX HAS BEEN COMPLETED

THIS FORM IS VALID ONLY DURING:

from 4/13/11 to 4/12/12

Date Last Revised: Version 4, Mar 2011



Subject Name: \_\_\_\_\_

Date: \_\_\_\_\_

Title of Study: Predictors of Treatment Response to Fluoxetine in PTSD Following a Recent History of War Zone Stress Exposure

Principal Investigator: Paul B. Hicks, MD, PhD

VAMC: CTVHCS

### Health Insurance Portability and Accountability Act of 1996 (HIPAA) Authorization

You have been asked to be part of a research study under the direction of the Principal Investigator, *Paul B. Hicks, MD, PhD*, and his research team. The purpose of this study is to determine whether the medication fluoxetine, often used to treat depression, is an effective treatment for posttraumatic stress disorder (PTSD) and associated conditions in soldiers and veterans with recent war-zone exposure, as well as determine whether any response to fluoxetine is related to the degree of trauma exposure, the severity of PTSD symptoms, resistance to psychological trauma, adequacy of social supports (family, extra-military and military), the degree of post-deployment stressors and life problems, or the degree of any loss of memory.

By signing this document you will authorize the Veterans Health Administration (VHA) to provide Paul B. Hicks, MD, PhD, and the authorized members of his research team, access to the following information about you.

- Demographic information (e.g., age, race, education, etc.) and military service (e.g., rank, the number of years in the Service, etc.)
- Medical History/Surgical History/History of Alcohol abuse and/or dependence/ History of Drug abuse and/or dependence
- Laboratory Results
- Responses to questionnaires and clinical interviews
- Frequency, duration, content, and type of therapy treatment sessions with your current Usual Care Clinician (therapist)
- Your name, social security number, date of birth, contact information

The Office for Human Research Protections (OHRP), Food and Drug Administration (FDA), Government Accounting Office (GAO), Veterans Health Administration (VHA), US Army Medical Research and Materiel Command (USAMRMC), other oversight agencies, the Research Compliance Officer, Institutional Review Board members or other research staff may have access to your research and/or medical records or may inspect the records. Data will be analyzed by an Associate Investigator at the VA Boston Healthcare System. Every effort will be made to keep information about you both private and confidential. Codes (not your name and/or social security number) will be used for all reports generated, to help maintain your confidentiality.

The disclosure of your protected health information is necessary in order to be able to conduct the research project described. Records of your participation in this study may only be disclosed in accordance with state and federal law, including the Privacy Act (5 U.S.C. 552a) and the Health Insurance Portability and Accountability Act of 1996 and its implementing regulations (45 CFR 160 & 164).

If you do not sign this authorization, you will not be part of the study. This authorization has no expiration date.





Subject Name: \_\_\_\_\_

Date: \_\_\_\_\_

Title of Study: Predictors of Treatment Response to Fluoxetine in PTSD Following a Recent History of War Zone Stress Exposure

Principal Investigator: Paul B. Hicks, MD, PhD

VAMC: CTVHCS

You can revoke this authorization at any time. To revoke your authorization, you can write to:

Paul B. Hicks, MD, PhD  
1901 South 1<sup>st</sup> Street (151)  
Temple, TX 76504

or you can ask a member of the research team to give you a form to revoke the authorization. If you revoke this authorization, you will not be able to continue to participate in the study. This will not affect your rights as a VHA patient.

If you revoke this authorization, Paul B. Hicks, MD, PhD and his research team can continue to use information about you that has already been collected. No information will be collected after you revoke the authorization.

The VHA complies with the requirements of the Health Insurance Portability and Accountability Act of 1996, its privacy regulations, and all other applicable laws that protect your privacy. We will protect your information according to these laws. Despite these protections, there is a possibility that your information could be used or disclosed in a way that it will no longer be protected. Our Notice of Privacy Practices (a separate document) provides more information on how we protect your information. If you do not have a copy of the Notice, the research team will provide one to you. You may contact the CTVHCS Privacy Officer, at 1-800-423-2111, ext. 42711 for additional information or questions regarding your privacy rights under the HIPAA Privacy Rules.

I have read this authorization form and have been given the opportunity to ask questions. If I have questions later, I understand I can contact *Paul B. Hicks, MD, PhD* at 254-743-2643. I will be given a signed copy of this authorization form for my records.

By signing this HIPAA Authorization Form, I authorize the use of my identifiable information as described above.

Participant's Signature \_\_\_\_\_

Date \_\_\_\_\_

Participant's Full Social Security Number \_\_\_\_\_

Signature of Person Obtaining Authorization \_\_\_\_\_

Date \_\_\_\_\_



## **Appendix C: No-Cost Extension of Award Contract**

<b>AMENDMENT OF SOLICITATION/MODIFICATION OF CONTRACT</b>				1. CONTRACT ID CODE <b>S</b>		PAGE OF PAGES <b>1   2</b>	
2. AMENDMENT/MODIFICATION NO. <b>P00002</b>		3. EFFECTIVE DATE <b>30-Jun-2010</b>		4. REQUISITION/PURCHASE REQ. NO. <b>W91ZSQ6289N640</b>		5. PROJECT NO.(If applicable)	
6. ISSUED BY USA MED RESEARCH ACQ ACTIVITY 820 CHANDLER ST FORT DETRICK MD 21702-5014		CODE <b>W81XWH</b>		7. ADMINISTERED BY (If other than item 6) USA MED RESEARCH ACQ ACTIVITY ATTN: AYI AYAYI 301-619-4018 AYI.AYAYI@AMEDD.ARMY.MIL FORT DETRICK MD 21702		CODE <b>W81XWH</b>	
8. NAME AND ADDRESS OF CONTRACTOR (No., Street, County, State and Zip Code) TEMPVA RESEARCH GROUP, INC. RESEARCH OFFICE (151N) 1901 S TEMPLE TX 76504-7451				9A. AMENDMENT OF SOLICITATION NO.			
				9B. DATED (SEE ITEM 11)			
				X 10A. MOD. OF CONTRACT/ORDER NO. <b>W81XWH-07-1-0283</b>			
				X 10B. DATED (SEE ITEM 13) <b>01-Jul-2007</b>			
CODE <b>362J2</b>		FACILITY CODE					
11. THIS ITEM ONLY APPLIES TO AMENDMENTS OF SOLICITATIONS							
<input type="checkbox"/> The above numbered solicitation is amended as set forth in Item 14. The hour and date specified for receipt of Offer <input type="checkbox"/> is extended, <input type="checkbox"/> is not extended. Offer must acknowledge receipt of this amendment prior to the hour and date specified in the solicitation or as amended by one of the following methods: (a) By completing Items 8 and 15, and returning _____ copies of the amendment; (b) By acknowledging receipt of this amendment on each copy of the offer submitted; or (c) By separate letter or telegram which includes a reference to the solicitation and amendment numbers. FAILURE OF YOUR ACKNOWLEDGMENT TO BE RECEIVED AT THE PLACE DESIGNATED FOR THE RECEIPT OF OFFERS PRIOR TO THE HOUR AND DATE SPECIFIED MAY RESULT IN REJECTION OF YOUR OFFER. If by virtue of this amendment you desire to change an offer already submitted, such change may be made by telegram or letter, provided each telegram or letter makes reference to the solicitation and this amendment, and is received prior to the opening hour and date specified.							
12. ACCOUNTING AND APPROPRIATION DATA (If required)							
13. THIS ITEM APPLIES ONLY TO MODIFICATIONS OF CONTRACTS/ORDERS. IT MODIFIES THE CONTRACT/ORDER NO. AS DESCRIBED IN ITEM 14.							
A. THIS CHANGE ORDER IS ISSUED PURSUANT TO: (Specify authority) THE CHANGES SET FORTH IN ITEM 14 ARE MADE IN THE CONTRACT ORDER NO. IN ITEM 10A.							
B. THE ABOVE NUMBERED CONTRACT/ORDER IS MODIFIED TO REFLECT THE ADMINISTRATIVE CHANGES (such as changes in paying office, appropriation date, etc.) SET FORTH IN ITEM 14, PURSUANT TO THE AUTHORITY OF FAR 43.103(B).							
C. THIS SUPPLEMENTAL AGREEMENT IS ENTERED INTO PURSUANT TO AUTHORITY OF:							
X D. OTHER (Specify type of modification and authority) IAW USAMRAA General Terms and Conditions							
E. IMPORTANT: Contractor <input checked="" type="checkbox"/> is not, <input type="checkbox"/> is required to sign this document and return _____ copies to the issuing office.							
14. DESCRIPTION OF AMENDMENT/MODIFICATION (Organized by UCF section headings, including solicitation/contract subject matter where feasible.) Modification Control Number: <b>aayayi105361</b> TITLE: <b>Predictors of Treatment Response to Fluoxetine in PTSD Following a Recent History of War Zone Stress Exposure</b> AWARD AMOUNT: <b>\$748,959</b>  1. The purpose of this modification is to extend the period of performance by 2 years at no cost in accordance with the recipient's request dated 03 June 2010, and the GOR's recommendation dated 09 June 2010. FROM: 01 July 2007 - 31 July 2010 (Research ends 30 June 2010) TO: 01 July 2007 - 31 July 2012 (Research ends 30 June 2012)  2. The final report is not due at this time. However, annual reports are due no later than 31 July in years 2010 and 2011. The final report is due no later than 31 July 2012.							
Except as provided herein, all terms and conditions of the document referenced in Item 9A or 10A, as heretofore changed, remains unchanged and in full force and effect.							
15A. NAME AND TITLE OF SIGNER (Type or print)				16A. NAME AND TITLE OF CONTRACTING OFFICER (Type or print) SUSAN DELLINGER / CONTRACT SPECIALIST TEL: 301-619-2090 EMAIL: susan.dellinger@amedd.army.mil			
15B. CONTRACTOR/OFFEROR  (Signature of person authorized to sign)		15C. DATE SIGNED		16B. UNITED STATES OF AMERICA BY <i>Susan M. Dellinger</i> (Signature of Contracting Officer)		16C. DATE SIGNED <b>30-Jun-2010</b>	

## SECTION SF 30 BLOCK 14 CONTINUATION PAGE

## SUMMARY OF CHANGES

## SECTION 00010 - SOLICITATION CONTRACT FORM

## CLIN 0001

The CLIN extended description has changed from GRANT - PRMRP Period of Performance: 1 Jul 07 - 31 Jul 10 (Research 30 Jun 10) to GRANT - PRMRP Period of Performance: 01 Jul 07 - 31 Jul 12 (Research 30 Jun 12).

## DELIVERIES AND PERFORMANCE

The following Delivery Schedule item for CLIN 0001 has been changed from:

DELIVERY DATE	QUANTITY	SHIP TO ADDRESS	UIC
POP 01-JUL-2007 TO 31-JUL-2010	N/A	USA MED RESEARCH AND MATERIEL COM 1077 PATCHEL STREET FORT DETRICK MD 21702 FOB: Destination	W91ZSQ

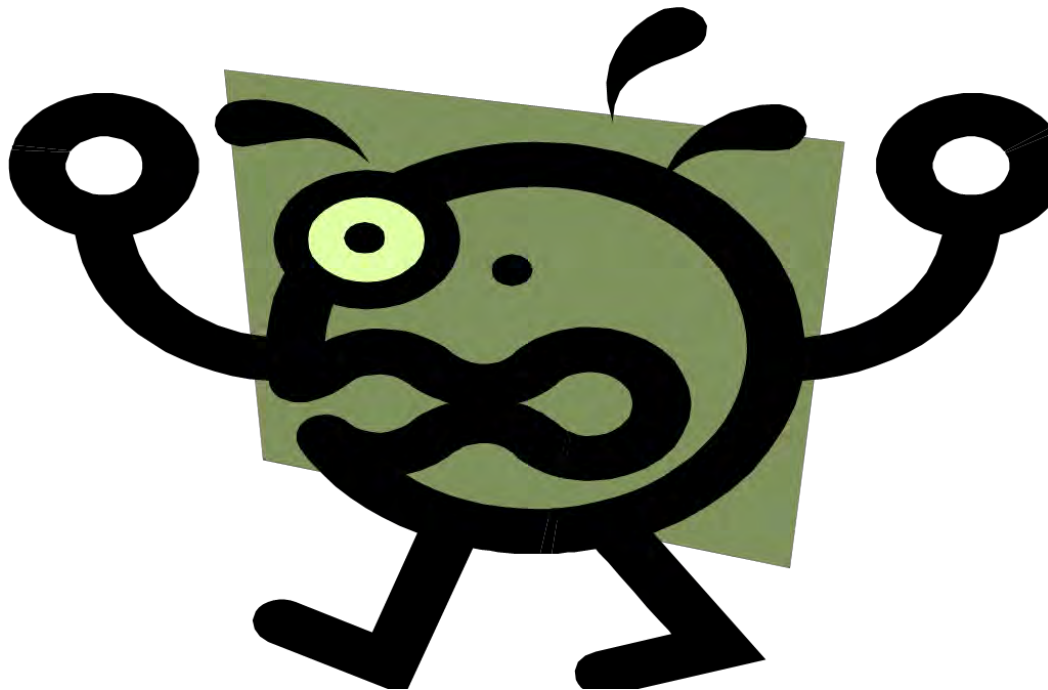
To:

DELIVERY DATE	QUANTITY	SHIP TO ADDRESS	UIC
POP 01-JUL-2007 TO 31-JUL-2012	N/A	USA MED RESEARCH MAT CMD 1077 PATCHEL STREET BLDG 1056 FORT DETRICK MD 21702 FOB: Destination	W91ZSQ

(End of Summary of Changes)

## **Appendix D: Recruitment Flyer**

**IRRITABLE?  
TROUBLE SLEEPING?  
FLASHBACKS?  
BAD DREAMS?  
FEELING EMOTIONALLY NUMB?**



The VA and the DOD are performing a clinical drug trial  
to improve treatment of PTSD.

If you were involved in a traumatic event during OEF/OIF,  
feel you may suffer from PTSD,  
and would consider participation in this study

call (254) 534-0370 or (254) 534-1044 for more information.

**LOCATION: between Resilience & Restoration Center (36003) and Urgent Care & Triage Clinic (36009)**

## **Appendix E: Recruitment Pamphlet**

ARE YOU  
IRRITABLE?



DO YOU HAVE  
TROUBLE  
SLEEPING....

AND/OR  
BAD DREAMS?

**Research Study  
Location:**

**Building 36003-B**

Between the  
Resilience &  
Restoration Center  
(36003) and the  
Urgent Care &  
Triage Clinic  
(36009)

"The views expressed in this pamphlet are those of the author and do not reflect the official policy or position of the Department of the Army, Department of Defense, or the U.S. Government. Opinions, interpretations, conclusions, and recommendations are those of the author and are not necessarily endorsed by the U.S. Army." AR 360-1

FEELING  
EMOTIONALLY  
NUMB?



EXPERIENCING  
INTRUSIVE  
THOUGHTS  
OR  
FLASHBACKS?



**If you are interesting in  
participating in this  
research project or would  
like additional information**



**The Central Texas  
Veterans Healthcare  
System  
and the  
Department of Defense**  
are performing a  
clinical drug trial  
to improve treatment of  
Posttraumatic Stress Disorder  
(PTSD).

*If you or someone you know are:*

- active duty military,
- had traumatic event  
during OEF or OIF, and
- feel you or they may be  
suffering from PTSD...

*consider learning more.*

**Hours of operation are  
0730 – 1600  
Monday thru Friday**

**No Appointment  
Or  
Referral needed!**

**Please contact us at  
(254) 534-0370  
Or  
(254) 534-1044**



**Or  
Visit us in  
Building 36003-B**